



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P825PC00	FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/DK2005/000160	International filing date (day/month/year) 09.03.2005	Priority date (day/month/year) 11.03.2004
International Patent Classification (IPC) or national classification and IPC INV. C12N15/82 A01H5/10 C12C1/18		
Applicant CARLSBERG AS		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 12 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau a total of 5 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input checked="" type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input checked="" type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand 20.03.2006	Date of completion of this report 24.01.2007	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tél. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Maddox, Andrew Telephone No. +31 70 340-2336 	

**INTERNATIONAL PRELIMINARY REPORT
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International application No.
PCT/DK2005/000160

Box No. I Basis of the report

1. With regard to the **language**, this report is based on
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-107 as originally filed

Sequence listings part of the description, Pages

1-27 received on 06.06.2005 with letter of 01.06.2005

Claims, Numbers

1-42 received on 13.10.2006 with letter of 11.10.2006

Drawings, Sheets

1/32-32/32 as originally filed

- ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify):*
 - ☐ any table(s) related to sequence listing *(specify):*
4. ☒ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☒ the claims, Nos. 31
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify):*
 - ☐ any table(s) related to sequence listing *(specify):*

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-3,5,9-28,32-42 all partially; 6-8 all completely

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*).
- ☒ no international search report has been established for the said claims Nos. 1-3,5,9-28,32-42 all partially; 6-8 all completely
- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:
- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.
- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☒ See separate sheet for further details

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has, within the applicable time limit:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest and, where applicable, the protest fee.
 - ☒ paid additional fees under protest but the applicable protest fee was not paid.
 - ☐ neither restricted the claims nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☒ complied with.
 - ☐ not complied with for the following reasons:
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-2,9-28,32-42 all partially, and 3-5 completely (claimed invention 1); 29-31 completely (claimed invention 3) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	4 12 13 15 19
	No: Claims	21-30
Inventive step (IS)	Yes: Claims	
	No: Claims	1-3, 5, 9-28, 32-42
Industrial applicability (IA)	Yes: Claims	1-5, 9-30, 32-42
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY REPORT
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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)
and /or
2. Non-written disclosures (Rule 70.9)
see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ on paper
 - ☒ in electronic form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed
 - ☐ filed together with the international application in electronic form
 - ☒ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment* on
 2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
 3. Additional comments:
- * If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

The following documents are relevant

- D1: WO 02/053720 A (CARLSBERG RESEARCH LABORATORY; HEINEKEN TECHNICAL SERVICES BV; BRASSER) 11 July 2002 (2002-07-11)
- D2: WO 02/053721 A (CARLSBERG RESEARCH LABORATORY; HEINEKEN TECHNICAL SERVICES BV; BRASSER) 11 July 2002 (2002-07-11)
- D3: WO 2004/085652 A (SAPPORO BREWERIES LIMITED; HIROTA, NAOHIKO; KANEKO, TAKAFUMI; CAIROTE,) 7 October 2004 (2004-10-07)
- D4: US 2003/167544 A1 (DOUMA ANNA CHRISTINA ET AL) 4 September 2003 (2003-09-04)
- D5: KURODA H ET AL: "Characterization of factors that transform linoleic acid into di- and trihydroxyoctadecenoic acids in mash" JOURNAL OF BIOSCIENCE AND BIOENGINEERING, ELSEVIER, AMSTERDAM,, NL, vol. 93, no. 1, 2002, pages 73-77, XP002980834 ISSN: 1389-1723
- D6: KOBAYASHI ET AL.: "Behavior of Mono-, Di-, and Trihydroxyoctadecenoic Acids during Mashing and Methods of Controlling Their Production" JOURNAL OF BIOSCIENCE AND BIOENGINEERING, vol. 90, no. 1, 2000, pages 69-73, XP002347966

The applicant has referred to the following documents

- A1: Kleinhofs, A., et al., Mutation Research 51 (1978), 29-35.
- A2: Robbins, M.P., et al., Plant Physiol. 116 (1998), 1133-1144.
- A3: Stahl, Y., et al., The Plant Journal 39 (2004), 599-611.

Re Item I

Basis of the report

- 1 The subject matter of claim 31 is not directly and unambiguously derivable from claims 35-37 as originally filed. The subject matter represents a combination of features not previously made available in the application as filed. Although the individual values of the claimed parameters are to be found on page 45 lines 3-4 and page 44 lines 2-6 there is no direct and unambiguous reference to the combination of both values. Although page 45 line 17-18 mentions that the beverage comprises

(i) a ratio of 9,12,13-THA to 9,10,13-THA as described above; and

(ii) a level of free T2N after storage described above

this is a generalisation and does not directly and unambiguously refer to the specific ratio of 1.8 combined with 0.05 ppm T2N when taken with the previous statements. Subject matter defined in a general manner does not disclose specific embodiments. In view of this fact the subject matter of claim 31 goes beyond the disclosure of the application as filed within the meaning of Article 34(2)(b) PCT. The examination is conducted as if this amendment had not taken place.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- 2 The application lacks unity of invention for the reasons mentioned in item IV (cf. infra). No additional search fee was paid for the subject matter of claimed invention 2 (cf. item IV) and has therefore not been examined in accordance with Rule 66.1(e) PCT.
- 2.1 The subject matter of claims 1-3, 5, 9-28 and 32-42 pertaining to claimed invention 1 (cf. Item IV) has only been searched in so far as it concerns the subject matter as defined in claim 4. The remaining unsearched subject matter underlying these claims has not been searched and hence not examined in accordance with Rule 66.1(e) PCT.

Re Item IV

Lack of unity of invention

- 3 The application relates to barley plants and beverages. The subject matter is linked by being related to barley derived beverages having stable organoleptic properties or the (barley plants for) production thereof. However such beverages have already been produced through the creation and use of mutant barley plants having reduced Lipoxygenase-1(LOX-1) enzyme activity, see for example WO02053720 (D1 - cf. examples) and WO02053721 (D2 - cf. examples). Both D1 & D2 (cf. claims 1, 17 and 20) further extend to barley plants absent in LOX-1 activity and the beer brewed therefrom. It is evident from D1 & D2 (cf. p. 1 lines 8-13; p. 5 lines 18-30; claim 3) that what is envisaged is a mutation in the LOX-1 gene that results in total loss-of-function. It is evident that a total loss of function in

the LOX1 gene will result in the production of a protein which can no longer be considered as a LOX1 protein. In other words the absence of LOX1 activity through a total loss of function can be equated as comprising essentially no LOX1 protein. This may also be derived from both D1 (cf. page 13 line 23) and D2 (cf. page 13 line 23) that envisage the abolition of LOX1 transcription. These features can therefore not be regarded as special technical features providing a common contribution over the state of the art within the meaning of Rule 13.2 PCT and shared by the whole claimed subject matter.

- 3.1 In light of D1 and D2 the application relates to different problems and corresponding solutions. The first technical problem is the provision of an alternative low-LOX-1 barley plant with a total loss-of-function in the LOX-1 gene and having essentially no LOX1 protein, two solutions are provided, firstly a barley plant with a nonsense mutation in the LOX-1 gene at positions 3572-3574 of SEQ ID NO:2 and secondly a barley plant with a splice site mutation of the LOX-1 gene at position 2311 of SEQ ID NO:6. The second technical problem is the provision of an alternative beverage with stable organoleptic properties. The solution is a barley derived beverage with a ratio of 9,12,13-trihydroxyoctadecenoic acid to 9,10,13-trihydroxyoctadecenoic acid of at most 1.8.
- 3.2 No further technical features that may be regarded as special within the meaning of Rule 13.2 PCT can be found linking these problems or their solutions, hence there is no single inventive concept underlying the alleged inventions within the meaning of Rule 13.1 PCT. Consequently there is a lack of unity and the different claimed inventions not belonging to a common inventive concept have been formulated as different subject matters as follows:

Claimed Invention 1: Claims 1-2,9-28,32-42 all partially; 3-5 all completely. Barley plant wherein the gene encoding LOX-1 of said plant comprises a nonsense codon corresponding to base nos. 3572-3574 of SEQ ID NO:2, methods and products based on said plant.

Claimed Invention 2: Claims 1-2,9-28,32-42 all partially; 6-8 all completely. Barley plant wherein the gene encoding LOX-1 of said plant comprises a splice site mutation said mutation corresponding to base no. 2311 of SEQ ID NO:6, methods and products based on said plant.

Claimed Invention 3: Claims 29-31 all completely. Beverage having stable organoleptic properties with a ratio of 9,12,13-trihydroxyoctadecenoic acid to 9,10,13-trihydroxyoctadecenoic acid of at the most 1.8.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 4 The preliminary examination is conducted on the subject matter of claimed Inventions 1 and 3 as mentioned in Item IV (cf. supra). The examination of the subject matter of claimed invention 1 has been restricted to that which relates by reference or dependency to the subject matter as defined by claim 4 (cf. Item III supra). For the sake of completeness the subject matter under examination in the case of claimed invention 1 is restricted to the barley plant which comprises a nonsense codon corresponding to base nos. 3572-3574 of SEQ ID NO:2 and that matter dependent on it or referring to it also restricted accordingly. The subject matter of claim 31 has not been considered in view of item I supra.
- 4.1 D1 (cf. examples) and D2 (cf. examples) both disclose beer beverages with stable organoleptic properties brewed using low-LOX barley. Both documents also foresee barley plants with no LOX-1 activity and the beer produced therefrom (cf. claims 1, 17 and 20). The subject matter of claim 21 relates to a beverage and not to a plant. The IPEA notes that the subject matter is directed to a product defined in terms of the process of manufacture. The IPEA is of the opinion that a beverage from a barley plant of claim 4 lacking LOX1 is not different from one manufactured from another LOX-1 absent plant or derived in any other manner in the absence of LOX1 activity. The fact that a barley plant of claim 4 may be novel does not confer novelty on a beverage (beer) defined in terms of being obtained therefrom in view of the fact that the distinguishing feature of the plant is neither incorporated into the beer directly nor determines the characteristics of the beer such that it is new with regard to the state of the art. The characterising feature of the beer of claim 21 is that it is produced in the absence of LOX-1 which leads to distinctive organoleptic properties. The beer produced using the plant of claim 4 lacking LOX1 will not be different to a beer produced in the absence of LOX1 as disclosed in D1 and D2. It is the opinion of the IPEA that with the common general knowledge, skill and ability of the relevant practitioner, that beer brewed without the presence of LOX-1 can be produced with or without first obtaining the plants of

claim 4. This may be achieved for example by the use of LOX-1 inhibitors or heat inactivation such as disclosed in D5 (cf. summary) or D6 (cf. summary) as techniques that would be known to the skilled person. Furthermore D5 clearly indicates the relevance of LOX-1 in particular to the production of trihydroxyoctadecenoic acids in the mash (cf. pages 75-77). The relevance of LOX2 and LOX3 is not discussed in D5. In the absence of any comparative analysis it follows that the inactivation of LOX1 as enabled by D5 yields beverages with the intrinsic properties of claim 21. The disclosure of the LOX1 sequences (SEQ ID NOS:8 & 10) in both D1 and D2 enables the production of antisense plants with no LOX1 activity as disclosed in D1 (cf. page 5 lines 21-24; page 13 line 29 - page 14 line 13) and D2 (cf. page 5 lines 21-24; page 13 line 29 - page 14 line 13). Furthermore both D1 (cf. page 13 line 23) and D2 (cf. page 13 line 23) provide for mutations in the promoter (cf. SEQ ID NO:8) that abolish transcription of LOX1. The IPEA also notes that any absence of LOX1 has essentially no LOX-1 protein in view of the fact that without LOX1 activity a protein may not be considered as a LOX1. The disclosures A2 and A3 concern the antisense regulation of other enzymes. The disclosures A2 and A3 do not concern the production of LOX-1 null mutants. The subject matter of claim 21 can therefore not be distinguished from the that brewed in D1 or D2 and is therefore not novel within the meaning of Article 33(3) PCT .

- 4.1.1 The objection of 5.1 applies *mutatis mutandis* to the subject matter of claims 22-28 as it does not add any new features to the beverage of claim 21 over that of D1 and D2.
- 4.2 The barley plant of claim 4 appears to be novel within the meaning of Article 33(2) PCT. It follows hereby that the subject matter of claims 12, 13, 15, and 19 is novel in so far as it relates to the plant of claim 4. However said subject matter appears to be derived plainly and logically from the teaching of either D1 or D2 as the skilled person would be aware of the need to reduce the levels of LOX-1 even further and would reasonably expect to find other mutations that achieved this goal. Said person would therefore have arrived at the subject matter of claim 4 by a process of routine experimentation devoid of any inventive skill or ability. The skilled person on reading D1 and D2, even if aware of other genes contributing to lipoxygenase activity, is nevertheless clearly taught from said document to reduce LOX-1 activity of plants to zero in response to improving organoleptic properties of beverages brewed therefrom. The skilled person being of a conservative nature

would therefore start from the position of reducing LOX-1 to zero. The problem underlying the application was the implementation of what had already been suggested in the state of the art D1 and D2, i.e. the production of total loss of LOX-1 activity. The skilled person would reasonably expect to find mutations in any enzyme that would lead to a total loss of activity or function. Indeed this is the basis of naturally occurring null mutations. In view of the fact that there are no apparent insurmountable difficulties foreseen or encountered by the skilled person in solving the problem, the solution provided by the applicant appears only to be a logical conclusion of the activities of the skilled person involved in addressing this problem. The IPEA can not find any reason to suggest that the skilled person would not reasonably expect to succeed in finding said mutations particularly as frameshift and nonsense mutations such as that underlying the subject matter of claim 4 are well known for completely destroying activity of encoded proteins. The fact that the screening method disclosed in D1 and D2 is difficult does not equate to the fact that it is impossible to obtain the null mutants of claim 4 in LOX-1 using routine methods, in fact the skilled person would have no reason to believe this task to be impossible and therefore would reasonably expect to succeed in obtaining the desired product. The document A1 relates to mutations in nitrate reductase. Nevertheless it notes the potential for creating loss of function mutants in barley. The fact that the skilled person embarking on the task prompted from D1 and D2 had no knowledge of the rate of success for lipoxygenase does not equate with a lack of reasonable expectation. Hence even if the method of the present application is more efficient than the methods disclosed in D1 or D2 then any inventive step lies in the specific method and not the products obtained by said method as said products may be produced by other means. The use of embryo or not in the screening method is not critical to obtaining the final product. Whether the effects related to the T2N or 9,12,13-THOE composition of beer are considered as bonus effects or not they remain intrinsic properties of the beverages that are clearly incited from D1 and D2 in relation to improving organoleptic properties. Moreover the relationship of this enzyme to the production of the THAs is not unexpected in view of both D5 (page 73; page 76 right col.) and D6 (cf. page 71 right col. - page 72 left col.) Notwithstanding this these effects relate to the solution of an unlinked problem (cf. item IV supra). Hence the subject matter of claim 4 does not involve an inventive step within the meaning of Article 33(3) PCT.

4.2.1 The remaining subject matter represented by claims 1-3, 5, 9-28, and 32-42

also lacks an inventive step within the meaning of Article 33(3) PCT as it concerns alternative embodiments derived directly from applying the teaching of either D1 or D2 to the subject matter of claim 4.

4.3 According to the present application (cf. p.7 l. 24 & 25; p. 44 l. 17 - p. 45 l.8) beverages prepared from barley which has no LOX-1 activity display very low levels of 9,12,13-THOE and thus a ratio of 9,12,13-THOE to 9,10,13-THOE of at the most 1.8. Barley beverages satisfying this ratio are anticipated in the state of the art. D1 and D2 (cf. claims 1, 17, and 20) disclose beer produced from a barley plant wherein LOX-1 Lipoxygenase activity is absent. D4 (cf. claims 1 and 24) discloses beer manufactured from a barley plant wherein LOX-1 Lipoxygenase activity is absent. The IPEA is of the opinion that this subject matter is reproducible given the state of the art and the skill and ability of the practitioner (cf. 5.1 supra) even without the plants of claim 4 as the skilled person would know how to produce beer without using LOX-1. As argued in 5.2 supra the claimed THOE ratio of a beer brewed without LOX-1 is an intrinsic property of that beer. Hence the subject matter of claims 29 and 30 is not novel within the meaning of Article 33(2) PCT.

5 Plant Variety

5.1 The subject matter of claim 8 concerns a plant variety within the meaning of Rule 67.1(ii) PCT. Nevertheless an examination has been undertaken notwithstanding the fact that this subject matter may be objected during prosecution of the application in the national or regional phase.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO2004/085652	07.10.2004	25.03.2004	25.03.2004

13.10.2003

(105)

What is claimed is:

1. A barley plant, or a part thereof, having a mutation in the LOX-1 gene causing a total loss-of-function, wherein said plant or part thereof comprises essentially no
5 LOX-1 protein.

2. The barley plant, or a part thereof, according to claim 1, wherein said part of said barley plant is kernel(s).

10 3. The barley plant, or a part thereof, according to claim 1 or 2, wherein the gene encoding LOX-1 of said plant comprises a premature nonsense codon.

4. The barley plant, or a part thereof, according to claim 3, wherein the gene encoding LOX-1 of said plant comprises a nonsense codon, said codon
15 corresponding to base no.s 3572–3574 of SEQ ID NO: 2.

5. The barley plant, or a part thereof, according to claim 3, wherein said plant is selected from the group consisting of plants designated D112 having American Type Culture Collection (ATCC) deposit accession No. PTA-5487, and progeny plants
20 thereof.

6. The barley plant, or a part thereof, according to claim 1 or 2, wherein the gene encoding LOX-1 of said plant comprises at least one mutation within a splice site.

25 7. The barley plant, or a part thereof, according to claim 6, wherein the gene encoding LOX-1 of said plant comprises a splice site mutation, said mutation corresponding to base no. 2311 of SEQ ID NO: 6.

8. The barley plant, or a part thereof, according to claim 6, wherein said plant is
30 selected from the group consisting of plants designated A618 having ATCC deposit accession No. PTA-5584, and progeny plants thereof.

9. The barley plant, or a part thereof, according to any of claims 1 to 8, wherein said plant is characterized by:

35 (i) having enhanced disease resistance; or

- (ii) having reduced potential for the production of mycotoxins; or
- (iii) comprising regenerable cells for use in tissue culture; or
- (iv) any combination of the traits of (i) to (iii).

5 10. The barley plant, or a part thereof, according to claim 9, wherein said LOX-1 gene comprises:

- (i) a premature nonsense codon; or
- (ii) a splice site mutation.

10 11. The barley plant according to claim 10, wherein said LOX-1 gene comprises:

- (i) a nonsense codon corresponding to base no.s 3572–3574 of SEQ ID NO: 2; or
- (ii) a splice site mutation corresponding to base no. 2311 of SEQ ID NO: 6.

15

12. A composition comprising the barley plant or part thereof according to any of claims 1 to 11.

20 13. A malt composition comprising a processed barley plant or part thereof, wherein said barley plant is the barley plant according to any of claims 1 to 11.

14. The malt composition according to claim 13, wherein said part of said barley plant is kernel(s).

25 15. A wort composition prepared using the barley plant or part thereof according to any of claims 1 to 11 or using a malt composition prepared from said barley plant or part thereof or mixtures thereof.

30 16. The wort composition according to claim 15, wherein said part of said plant is kernel(s).

17. The wort composition according to claim 15, wherein said malt composition is a malt composition according to any of claims 13 and 14.

18. The wort composition according to any of claims 15 to 17, wherein said composition is prepared using an enzyme composition or an enzyme mixture composition.

5 19. A composition prepared from a mixture of (i) a composition comprising a barley plant or a part thereof according to any of claims 1 to 11 , and (ii) a malt composition according to any of claims 13 and 14.

10 20. A wort composition or a beverage prepared from the composition of claim 19.

21. A beverage having stable organoleptic qualities, wherein said beverage is obtained by manufacturing the barley plant or part thereof according to any of claims 1 to 11.

15 22. The beverage according to claim 21, wherein said beverage is beer.

23. The beverage according to claim 21, wherein said beverage is prepared using malt prepared from kernels of said barley plant.

20 24. The beverage according to any of claims 21 to 23, wherein said beverage is prepared from a wort composition prepared from a barley plant or part thereof, or from a malt composition prepared from said barley plant or part thereof

25 25. The beverage according to claim 21, wherein said beverage is prepared from unmalted barley plants or parts thereof.

26. The beverage according to any of claims 21 to 25, wherein said beverage is a non-fermented beverage

30 27. The beverage according to any of claims 21 to 26, wherein said barley plant, or parts thereof, comprise a LOX-1 gene, said gene comprising:

- (i) a nonsense codon; or
- (ii) a splice site mutation.

28. The beverage according to claim 27, wherein the gene encoding LOX-1 comprises:

- (i) a nonsense codon, said codon corresponding to base no.s 3572–3574 of SEQ ID NO: 2; or
- 5 (ii) a splice site mutation, said mutation corresponding to base no. 2311 of SEQ ID NO: 6.

29. A beverage having stable organoleptic qualities, wherein said beverage is manufactured by using a barley plant, wherein the ratio of
10 9,12,13-trihydroxyoctadecenoic acid to 9,10,13-trihydroxyoctadecenoic acid within said beverage is at the most 1.8.

30. The beverage according to any of claims 28 to 29, wherein said beverage is beer.
15

31. The beverage of claim 29 or 30, wherein said beverage comprises at the most 0.05 ppb free *trans*-2-nonenal (T2N) after incubation at 37°C for 4 weeks, in the presence of in the range of 4 to 6 ppm sulfite.

20 32. A plant product produced from the barley plant, or a part thereof, according to any of claims 1 to 11.

33. The plant product according to claim 32, wherein said plant product is a beverage.
25

34. A method of producing:

- (i) a food composition; or
 - (ii) a feed composition; or
 - (iii) a fragrance raw material composition; or
 - 30 (iv) any combination of (i) to (iii);
- using a barley plant or part thereof according to any of claims 1 to 11.

35. A food composition, a feed composition, or a fragrance raw material composition comprising the barley plant or part thereof according to any of claims 1 to 11.
35

36. A method for expressing a recombinant protein in barley to obtain a barley plant according to any of claims 1 to 11, wherein said method comprises stably transforming said plant with a nucleic acid sequence comprising, as operably linked components, a promoter expressable in barley plants or parts thereof, a DNA
5 sequence encoding said recombinant protein, and a transcriptional termination region.

37. A method of producing a beverage having stable organoleptic qualities, said method comprising the steps of:
10 (i) preparing a composition comprising a barley plant or parts thereof according to claim 1;
(ii) processing the composition of (i) into a beverage;
thereby obtaining a beverage with stable organoleptic qualities.

15 38. The method according to claim 37, wherein step (i) comprises preparing a malt composition from kernels of said barley plant or part thereof.

39. The method according to any of claims 37 and 38, wherein the method further comprises incubation with a LOX inhibitor.
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40. The method according to claim 37, wherein processing the composition into a beverages comprises a mashing step.

41. The method according to claim 37, wherein a LOX inhibitor is added during said
25 mashing step.

42. A method of producing a malt composition with low or no LOX-1 activity, said method comprising the steps of:
30 (i) providing kernels according to claim 2;
(ii) steeping said kernels;
(iii) germinating the steeped kernels under predetermined conditions;
(iv) treating germinated kernels with heat;
thereby producing a malt composition with no or low LOX-1 activity.

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